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TITLE: Nematode-extracted anticoagulant protein.

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US-CL-CURRENT: 514/12; 530/324, 530/350

CLAIMS:

We claim:

1. An isolated protein having serine protease inhibitory activity and having one or more Nematode-extracted Anticoagulant Protein domains ("NAP domains"), wherein each NAP domain includes the sequence:
Cys-A1-Cys-A2-Cys-A3-Cys-A4-Cys-A5-Cys-A6-Cys-A7-Cys-A8-Cys-A9-Cys-A10, wherein
(a) A1 is an amino acid sequence of 7 to 8 amino acid residues;
(b) A2 is an amino acid sequence;
(c) A3 has the sequence Glu-A3.sub.a -A3.sub.b, wherein A3.sub.a and A3.sub.b are independently selected amino acid residues.
(d) A4 is an amino acid sequence having a net anionic charge;
(e) A5 has the sequence A5.sub.a -A5.sub.b -A5.sub.c wherein A5.sub.a through A5.sub.c are independently selected amino acid residues;
(f) A6 is an amino acid sequence;
(g) A7 is Gln;
(h) A8 is an amino acid sequence of 10 to 12 amino acid residues;
(i) A9 is an amino acid sequence of 5 to 7 amino acid
(j) A10 is an amino acid sequence;
wherein each A2, A4, A6 and A10 has an independently selected number of independently selected amino acid residues and each sequence is selected such that each NAP domain has in total less than about 120 amino acid residues and wherein said isolated protein is derived from a hematophagous nematode species.
2. The protein of claim 1, wherein A3 is Glu-Pro-Lys.
3. The protein of claim 1, wherein A5.sub.a is Thr and A5.sub.b is Asn.
4. The protein of claim 3, wherein A5 is selected from Thr-Ileu-Asn and Thr-Met-Asn.
5. The protein of claim 1, wherein said nematode species is selected from the group consisting of *Angiostrongylus cantonicus*, *Angiostrongylus brasiliensis*, *Angiostrongylus duodenalis*, *Necator americanus*, and *Heligmosomoides polygyrus*.
6. The protein of claim 1 having a NAP domain with an amino acid sequence selected from a sequence of a NAP domain of HpoNAP5 (SEQ. ID. NO. 65) and a NAP domain of NamNAP (SEQ. ID. NO. 61).

7. The protein of claim 1, wherein said nematode species is selected from the group consisting of *Ancylostoma caninum*, *Ancylostoma ceylanicum*, *Ancylostoma duodenale*, *Necator americanus*, and *Heligmosomoides polygyrus*.
8. The protein of claim 1, wherein:
 - (a) A3 is Glu-Pro-Lys; and
 - (b) A5 is selected from Thr-Leu-Asn and Thr-Met-Asn.
9. The protein of claim 8 having a NAP domain with an amino acid sequence selected from a sequence of a NAP domain of HpcNAP5 (SEQ. ID. NO. 60) and a NAP domain of NamNAP (SEQ. ID. NO. 61).
10. The protein of claim 8, wherein said nematode species is selected from the group consisting of *Ancylostoma caninum*, *Ancylostoma ceylanicum*, *Ancylostoma duodenale*, *Necator americanus*, and *Heligmosomoides polygyrus*.
11. A pharmaceutical composition comprising the protein of claim 1.
12. A pharmaceutical composition comprising the protein of claim 7.
13. A pharmaceutical composition comprising the protein of claim 8.
14. A method of inhibiting a serine protease comprising administering an effective amount of a protein of claim 1 with a pharmaceutically acceptable carrier.
15. A method of inhibiting a serine protease comprising administering an effective amount of a protein of claim 7 with a pharmaceutically acceptable carrier.
16. A method of inhibiting a serine protease comprising administering an effective amount of a protein of claim 8 with a pharmaceutically acceptable carrier.
17. A protein of claim 1, wherein said protein has two NAP domains.
18. A protein of claim 7, wherein said protein has two NAP domains.
19. A protein of claim 8, wherein said protein has two NAP domains.
20. An isolated protein having serine protease inhibitory activity and a NAP domain with an amino acid sequence selected from the group consisting of a sequence of a NAP domain of HpcNAP5 (SEQ. ID. NO. 60) and a NAP domain of NamNAP (SEQ. ID. NO. 61).
21. A pharmaceutical composition comprising a protein selected from the group consisting of HpcNAP5 (SEQ. ID. NO. 60) and NamNAP (SEQ. ID. NO. 61).
22. A method of inhibiting a serine protease comprising administering an effective amount of a protein selected from the group consisting of HpcNAP5 (SEQ. ID. NO. 60) and NamNAP (SEQ. ID. NO. 61).